Evaluation of Human Brain Tumor Angiogenesis Using Simultaneously-Acquired Gradient-Echo & Spin-Echo EPI During Dynamic Susceptibility Contrast

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Introduction The combination of high-speed MRI, and magnetic susceptibility contrast enables the acquisition of relative cerebral blood volume (rCBV) maps. Preliminary results (1) suggest that the rCBV maps obtained from patients with brain tumors may provide information about tumor vessel growth (angiogenesis), which plays a key role in tumor growth, malignancy and drug delivery.

Recently, it was demonstrated in a rat tumor model that the ratio of gradient-echo (GE) and spin-echo (SE) relaxation rate changes ($\Delta R2^*/\Delta R2$) may provide additional information about tumor vascular morphology (2). In particular, this ratio, determined in the presence of a long-lived iron-oxide agent, was significantly greater for tumor than contralateral normal brain. Since SE sequences are maximally sensitive to capillary-sized compartments, while GE sequences are equally sensitive to all vessel sizes, these results suggest a greater relative density of large versus small vessels in tumor relative to brain, a finding that correlated well with the histologic analyses.

The purpose of this study was to simultaneously-acquire GE rCBV, SE rCBV and $\Delta R2^*/\Delta R2$ information in patients with suspected brain neoplasms, with the goal of providing information about both blood volume and vascular morphology. The approach entailed simultaneously acquiring GE and SE images during the first pass of a magnetic susceptibility contrast agent.

Methods Three patients were studied on a 1.5T GE Signa System fitted with a 12" local three axis gradient coil and a quadrature transmit-receive birdcage RF coil (Medical Advances, Milwaukee WI). After collecting high resolution anatomical images, a 0.05mmole/kg loading dose of Gadoteridol (ProHance) was administered to diminish T1 effects that might result from agent extravasation. Near-simultaneous GE/SE images using single shot blipped EPI (3) were acquired for 1 min before and 2 mins after a 0.2 mmole/kg bolus injection. Five, 7mm slices were acquired at GE and SE TEs = 30ms and 109.1ms with TR = 1s and a FOV = 24cm.

To create GE rCBV maps, the GE signal versus time data was converted to T2* relaxation rate changes ($\Delta R2^* = \Delta(1/T2^*)$) as follows:

$$\Delta R2^*(t) = \frac{-1}{TE} \ln\left(\frac{S_c(t)}{S_b}\right) \qquad (1)$$

where $S_c(t)$ is the post-contrast GE signal at time t, and S_b is the averaged pre-contrast baseline signal. Similarly, T2 relaxation rate changes ($\Delta R2(t)$) were computed from the SE signal. The GE and SE rCBV maps were generated by integrating the $\Delta R2^*(t)$ and $\Delta R2(t)$ data on a pixelwise basis from the injection time to the end of image acquisition. Ratio maps were created from which an averaged (over time) post-contrast $\Delta R2^*/\Delta R2$ image was determined. From the rCBV and ratio maps, ROIs were chosen to cover areas containing the suspected neoplasm and corresponding contralateral brain tissue. The rCBV and $\Delta R2^*/\Delta R2$ data, presented in histogram form, were extracted from these brain and 'tumor' ROIs.

Results / Discussion From the three studies, one data set was uninterpretable because of severe motion. Of the remaining two, histologic examination of Patient A confirmed a diagnosis of malignant lymphoma. MR spectroscopic results (4) from Patient B, with a history of Grade II astrocytoma, are consistent with a recurrent neoplastic process.

Representative histograms of rCBV and ratio results from both brain and tumor ROIs are given in Figs 1 and 2. For both patients both GE and SE tumor rCBV values were consistently less and more homogenous than normal contralateral brain. (No significant agent extravasation was apparent in these studies; so the lower rCBVs cannot be attributed to a competing T1 effect.) Alternatively, the $\Delta R2^*/\Delta R2$ was either the same as contralateral brain or in several cases greater and more heterogeneous as illustrated in Fig. 2. This finding is consistent with previous studies (2) suggesting larger sized vessels in tumor relative to normal brain.

To begin addressing issues regarding the possible influence of parameters other than vessel size on $\Delta R2^*/\Delta R2$, the ratios are plotted as a function of GE and SE rCBV in Fig. 3. Both brain and tumor ratios increase with GE rCBV with a strong correlation for brain (R = 0.78) and much weaker dependence for tumor (R = 0.31). No dependence on SE rCBV was observed for either brain (R=0.12) or tumor (R=0.04). Why little correlation with ratio is observed for tumor is presently unclear, but may be due to tissue differences that also influence susceptibility contrast e.g. vascular topology. The lack of correlation between ratio and SE rCBV may be due to several competing effects. For example, decreases in $\Delta R2$ resulting from larger vessel sizes may compete with the presence of more small compartments (red blood cells) and increased blood volumes acting to increase $\Delta R2$. Clearly, before $\Delta R2^*/\Delta R2$ can become a useful indicator of averaged vessel size the significance of effects such as vascular volume weighting, organization and intra and extravascular effects must be fully characterized.

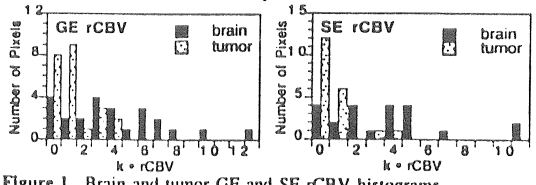

Figure 1. Brain and tumor GE and SE rCBV histograms.

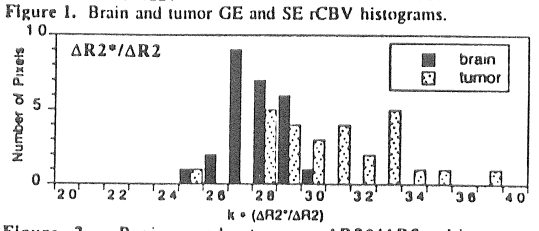

Figure 2. Brain and tumor $\Delta R2^*/\Delta R2$ histograms.

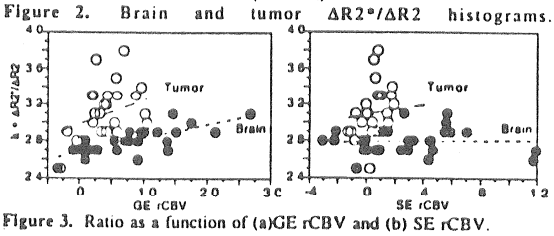

Figure 3. Ratio as a function of (a)GE rCBV and (b) SE rCBV.

Conclusion These studies demonstrate that the simultaneous acquisition of SE and GE images during dynamic susceptibility contrast agent passage, has the potential to provide specific information relevant to tumor angiogenesis.

References

1. Aronen H.J. et. al., *Radiology*, 191:41-51 (1994).
2. Dennie J. et. al., *ISMRM*, Vancouver (1997), p 489.
3. Bandettini P.A., et. al., *12th SMRM*, 169 (1993).
4. Rand S., Prost R. et. al., *Am J Neuro Rad*, 1997 (in press).

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